

**Amendments to the Claims:**

This listing of claims will replace all prior versions, and listings, of claims in the application:

**Listing of Claims:**

1. (Previously presented) A method of regulating cytotrophoblast differentiation and migration, the method comprising regulating the competition for binding to the cation independent mannose-6-phosphate (CIM6P) receptor between IGF-II and latent TGF- $\beta$  by administration of a differentiation factor selected from the group consisting of IGF-II, an IGF-II analogue and an antibody specific against latent TGF- $\beta$  to thereby promote the interaction between said IGF-II and said CIM6P.

2. (Previously presented) A method of promoting the implantation of an embryo in the uterine decidual endometrium, the method comprising regulating the competition for binding to the cation independent mannose-6-phosphate (CIM6P) receptor between IGF-II and latent TGF- $\beta$  by administration of a differentiation factor selected from the group consisting of IGF-II, an IGF-II analogue and an antibody specific against latent TGF- $\beta$  to thereby promote the interaction between said IGF-II and said CIM6P.

3. (Previously presented) The method of claim 2, wherein said differentiation factor is administered to an embryo produced by in vitro fertilization.

4. (Previously presented) The method of claim 2, wherein said differentiation factor is administered to a pregnant female subject in need thereof.

5. (Previously presented) The method of claim 2, wherein said differentiation factor is administered to a pregnant female subject in the first half of pregnancy.

6. (Previously presented) The method of claim 2, wherein said differentiation factor is administered to an embryo while maintaining said embryo in a relatively hypoxic environment.

7. (Previously presented) The method of claim 2, wherein said embryo comprises a mammalian embryo selected from the group consisting of a human, horse, cow, pig, goat and sheep.

8. (Withdrawn) A method of preventing the implantation of an embryo in the uterine decidual endometrium, the method comprising regulating the competition for binding to the cation independent mannose-6-phosphate (CIM6P) receptor between IGF-II and latent TGF- $\beta$  by

administration of a differentiation factor selected from the group consisting of latent TGF- $\beta$ , a TGF- $\beta$  analogue and an antibody specific against IGF-II that inhibit the interaction between IGF-II and CIM6P.

9. (Withdrawn) A method of regulating differentiation and migration of embryonic stem cells or adult stem cells, the method comprising regulating the competition for binding to the cation independent mannose-6-phosphate (CIM6P) receptor between IGF-II and latent TGF- $\beta$  by administration of an differentiation factor selected from the group consisting of IGF-II, an IGF-II analogue and an antibody specific against latent TGF- $\beta$  that promote the interaction between IGF-II and CIM6P.

10. (Withdrawn) A method of promoting terminal differentiation of embryonic stem cells or adult stem cells, the method comprising regulating the competition for binding to the cation independent mannose-6-phosphate (CIM6P) receptor between IGF-II and latent TGF- $\beta$  and exposing said cells to reduced levels of IGF-II, whereby the stem cell CIM6P receptors are able to bind latent TGF- $\beta$  and thereby promote the activation of TGF- $\beta$ .

11. (Withdrawn) A method of promoting stem cell division and stem cell migration, the method comprising regulating the competition for binding to the cation independent mannose-6-phosphate (CIM6P) receptor between IGF-II and latent TGF- $\beta$  and exposing said cells to increased levels of IGF-II, whereby the stem cell CIM6P receptors are unable to bind latent TGF- $\beta$  and thereby inhibiting the activation of TGF- $\beta$ .

12. (Withdrawn) A method of diagnosing a predisposition of cytotrophoblast cells or stem cells to differentiate and migrate, the method comprising determining in a mother, father or an embryo the presence of a polymorphic form of a gene wherein the level of expression of said gene serves to regulate the competition for binding to the cation independent mannose-6-phosphate (CIM6P) receptor between IGF-II and latent TGF- $\beta$  and, whereby the CIM6P receptors have altered ability to bind latent TGF- $\beta$  and thereby altered ability to activate TGF- $\beta$ .

13. (Withdrawn) The method of claim 12, wherein said gene is selected from the group consisting of an insulin-like growth factor II gene, a urokinase plasminogen activator gene, a urokinase plasminogen activator receptor gene, a CIM6P (type-2 IGF) receptor gene, a TGF- $\beta$  gene, a plasminogen gene and any polymorphic forms thereof.

14. (Withdrawn) A method of diagnosing a predisposition of cytotrophoblast cells to differentiate and migrate, the method comprising determining in a mother, father or embryo the

sequence of nucleotides in the DNA near the insulin-like growth factor II gene to thereby determine the capacity of the cytotrophoblast to migrate into the uterine decidua and the capacity of the placenta to transport substrates to the embryo, said insulin-like growth factor II gene comprising the insulin (INS) variable number of tandem repeats (VNTR).

15. (Withdrawn) A method of determining the ability of cytotrophoblast cells to differentiate and migrate, the method comprising measuring the amount of messenger RNA transcribed from the insulin-like growth factor II gene in an embryo.

16. (Withdrawn) A method of determining the ability of cytotrophoblast cells to differentiate and migrate, the method comprising measuring the amount of insulin-like growth factor II protein secreted by a mammalian embryo.

17. (Withdrawn) A method of determining the ability of cytotrophoblast cells to differentiate and migrate, the method comprising measuring the amount of insulin-like growth factor II protein circulating in maternal and paternal blood.